Please delete the paragraph on page 23, line 18, to page 24, line 15, and replace it with the following paragraph:

"Glutamate transporter" is used herein to refer to transmembrane proteins that remove L-glutamate, the primary excitatory neurotransmitter in the mammalian central nervous system (CNS), from the extracellular space, including the synaptic cleft and extrasynaptic space. Glutamate transporters may be found in the membranes of both neurons and glial cells. Several glutamate transporters have been identified in humans and include, for example, Solute Carrier family 1, member 1 (SLC1A1 or EAAC1 or EAAT3; for example GenBank Accession No.:NM_004170 **(Nucleotide and amino acid sequences are shown in SEQ ID NOS 3 and 4, respectively)**), Solute Carrier family 1, member 2 **(Nucleotide and amino acid sequences are shown in SEQ ID NOS 5 and 6, respectively),** (SLC1A2 or EAAT2 or GLT1; for example GenBank Accession No.:NM_004171), Solute Carrier family 1, member 3 (SLC1A3 or EAAT1, GLAST or GLAST1; for example GenBank Accession No.:NM_004172 **(Nucleotide and amino acid sequences are shown in SEQ ID NOS 7 and 8, respectively)**), Solute Carrier family 1, member 6 (SLC1A6 or EAAT4; for example GenBank Accession No.:NM_005071 **(Nucleotide and amino acid sequences are shown in SEQ ID NOS 9 and 10, respectively)**) and Solute Carrier family 1, member 7 (SLC1A7 or EAAT5; for example GenBank Accession No.:NM_006671 **(Nucleotide and amino acid sequences are shown in SEQ ID NOS 11 and 12, respectively)**). Further, glutamate transporters have been identified in *Rattus norvegicus* and *Mus musculus* (Slc1a1/Eaac1/REAAC1, Slc1a2/GluT/GLT-1/GluT-R, Slc1a3/Eaat1/GLAST/GluT-1 and Slc1a6/Eaat4). Homologs of the foregoing are believed to exist in other mammals, including primates, canines, felines and rodents. The activity of a glutamate transporter protein is increased by administration of an agent that increases glutamate transporting activity of a glutamate transporter protein. Examples of agents reported to increase glutamate transport protein activativity include, for example, ((R)-(-)-5-methyl-1-nicotinoyl-2-pyrazoline (MS-153; Shimada et al., Eur J Pharmacol. 386:263-70, 1999); lidocaine (Do et al., Anesth Analg. 95:1263-8, 2002) and kinase inhibitors (e.g., Conradt, J Neurochem. 68:1244-51, 1997).

Please delete the paragraph on page 25, line 1, to page 26, line 12, and replace it with the following paragraph:

"Metabotropic glutamate receptor" (mGluR) is used herein to refer to the G protein-coupled receptors that respond to the neurotransmitter glutamate. Based upon their primary sequence similarity, signal transduction linkages and pharmacological profile, there are three groups of mGluR's. Group I consists of mGluR1 (mGluR1a, mGluR1b, mGluR1c, mGluR1d; e.g., GenBank Accession number NM_000838 **(Nucleotide and amino acid sequences are shown in SEQ ID NOS 13 and 14, respectively)** for human splice variant mGluR1a) and mGluR5 (mGluR5a, mGluR5b; e.g., GenBank Accession number NM_000842 **(Nucleotide and amino acid sequences are shown in SEQ ID NOS 15 and 16, respectively)** for human splice variant mGluR5a) that are positively coupled to phospholipase C. Group II consists of mGluR2 (e.g., GenBank Accession number NM_000839 **(Nucleotide and amino acid sequences are shown in SEQ ID NOS 17 and 18, respectively)**) and mGluR3 (e.g., GenBank Accession number NM_000840 **(Nucleotide and amino acid sequences are shown in SEQ ID NOS 19 and 20, respectively)**) that are negatively linked to adenyl cyclase. Group II consists of mGluR4 (mGluR4a, mGluR4b; e.g., GenBank Accession number NM_000841 **(Nucleotide and amino acid sequences are shown in SEQ ID NOS 21 and 22, respectively)**), mGluR6 (e.g., GenBank Accession number NM_000843 **(Nucleotide and amino acid sequences are shown in SEQ ID NOS 23 and 24, respectively)**), mGluR7 (mGluR7a, mGluR7b; e.g., GenBank Accession number NM_000844 **(Nucleotide and amino acid sequences are shown in SEQ ID NOS 25 and 26, respectively)** for the human splice variant of mGluR7a) and mGluR8 (e.g., GenBank Accession number NM_000845 **(Nucleotide and amino acid sequences are shown in SEQ ID NOS 27 and 28, respectively)**) that are negatively linked to adenyl cyclase. There are a number of commercially available agonists and antagonists for the various mGluR groups. For example, Group I agonists include but are not limited to L-quisqualic acid ((L)-(+)-α-amino-3,5-dioxo-1,2,4-oxadiazolidine-2-propanoic acid), (S)-3,5-dihydroxyphenylglycine ((S)-3,5-DHPG), trans-azetidine-2,4-dicarboxylic acid (tADA), (1S,3R)-1-aminocyclopentane-1,3-dicarboxylic acid ((1S,3R)-ACPD) and (RS)-2-Chloro-5-

hydroxyphenylglycine (CHPG); and antagonists include but are not limited to (S)-4-carboxy-3-hydroxyphenylglycine ((S)-4C3HPG), 7-(hydroxyimino)cyclopropa[b]chromen-1a-carboxylate ethyl ester (CPCCOEt), (RS)-1 aminoindan-1,5-dicarboxylic acid (AIDA; UPF 523), 2-methyl-6-(phenylethynyl)pyridine (MPEP hydrochloride), 2-methyl-6-(2-phenylethenyl) pyridine (SIB-1893), 6-methyl-2-(phenylazo)-3-pyridinol (SIB-1757), and (S)-(+)-α-amino-4-carboxy-2-methylbenzeneacetic acid (LY 367385). Group II agonists include (2S,2′R,3′R)-2-(2′,3′-dicarboxycyclopropyl)glycine (DCG IV), (2S,1′S,2′S)-2-(carboxycyclopropyl)glycine (L-CCG-I; (2S,3S,4S)-CCG), (S)-3 carboxy-4-hydroxyphenylglycine ((S)-3C4HPG) and (2R,4R)-4-aminopyrrolidine-2,4-dicarboxylate ((2R,4R)-APDC); and antagonists include (2S)-α-Ethylglutamic acid (EGLU) and (2S)-2-amino-2-[(1S,2S)-2-carboxycycloprop-1-yl]-3-(xanth-9-yl) propanoic acid (LY 341495). Group III agonist include (1S,3R,4S)-1-aminocyclopentane-1,2,4-tricarboxylic acid (ACPT-I), L(+)-2-amino-4-phosphonobutyric acid (L-AP4), (R,S)-4-phosphonophenylglycine ((R,S)-PPG) and O-phospho-L-serine (L-SOP); and antagonists include (RS)-α-Cyclopropyl-4-phosphonophenylglycine (CPPG), (S)-2-amino-2-methyl-4-phosphonobutanoic acid (MAP4) and (RS)-α-Methylserine-O-phosphate (MSOP). Recent evidence has shown that metabotropic glutamate receptors associated with glia can alter the expression of glutamate transporters (Aronica et al., Eur. J. Neurosci. 2003; 17: 2106-18, 2003).

Please delete the paragraph on page 105, lines 9-13, and replace it with the following paragraph:

A probe set on the microarray was an identified gene for pituitary adenyl cyclase activator polypeptide (PACAP; GenBank Accession No.: AI227715; EST224410 **(SEQ ID NO: 29)**), that regulates glutamate transport and metabolism (Figiel and Engele, J. Neurosci. 15: 3596-3605, 2000). PACAP mRNA was significantly elevated in aged unimpaired relative to comparison young and aged impaired rats (Effect size 3.29, $t=4.13$, $p<.005$; Figure 4).

Please delete the paragraph on page 105, lines 14-20, and replace it with the following paragraph:

Because PACAP receptors are of a type that exhibit desensitization, a strong increase in β-arrestin 2 mRNA may participate in effects on glutamate tranporters. Beta-arrestin 2 has a dual role

in receptor endocytosis and in mediating signaling cascades through the same receptors (Wei et al., PNAS, 100;10782-7, 2003; Ahn et al., PNAS, 100;1740-4, 2003; e.g. GenBank Accession No.: XM_345084 **(Nucleotide and amino acid sequences are shown in SEQ ID NOS 30 and 31, respectively)**). The probe sets for β-arrestin 2 in the aged unimpaired rats showed significant elevation relative to comparison young and aged impaired (Effect size = 2.78, t=2.59, p<.05).

Please delete Table II on page 108, and replace it with the following Table:

Table II

	GLT-1	**EAAC1**	**GLAST**
PCR product	405bp	409bp	441bp
Sense	5'-GAGCATTGGTG CAGCCAGTA-3' **(SEQ ID NO: 32)**	5'-GTCTGAGAACA AGACAAAGG-3' **(SEQ ID NO: 33)**	5'-GGTAGAAGCCT GCTTTAAAC-3' **(SEQ ID NO: 34)**
Antisense	5'-CCAAGGTTCTTCC TCAACAC-3' **(SEQ ID NO: 35)**	5'-TGAGAGCTGTCA GGAGAGC-3' **(SEQ ID NO: 36)**	5'-GGCATGAATGAG GAGGCCGAC-3' **(SEQ ID NO: 37)**
Extended SP6 Sense	5'-tatttaggtgacactatagGAGCA TTGGTGCAGCCAGTA-3' **(SEQ ID NO: 38)**	5'-tatttaggtgacactatagGTCT GAGAACAAGACAAAG G-3' **(SEQ ID NO: 39)**	5'-tatttaggtgacactatag GGTA GAAGCCTGCTTTAAAC-3' **(SEQ ID NO: 40)**
Extended T7 Sense	5'taatacgactcactatagggCCAA GGTTCTTCCTCAAC-3' **(SEQ ID NO: 41)**	5'taatacgactcactatagggTGA GAGCTGTCAGGAGAG C-3' **(SEQ ID NO: 42)**	5'-taatacgactcactatagggGG CATGAATGAGGAGGCCG AC-3' **(SEQ ID NO: 43)**

Please delete the paragraph on page 112, lines 17-22, and replace it with the following paragraph:

For GLT1 the optimal reaction conditions were 0.6Units Platinum Taq DNA polymerase, 20mM Tris-HCl (pH 8.4), 50 mM KCl, 200μM dGTP, 200μM dATP, 200μM dCTP, 400μM dUTP, 0.4Units UDG, 6.0mM MgCl2, 50nM Forward primer, 200nM Reverse primer, 50nM probe. The amplicon length was 65 bps. The forward primer was 5' GAG CTG GAC ACC ATT GAC TC 3'